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Correlation of clinical and neurophysiological findings with health-related quality of life in patients with diabetic polyneuropathy

Korelacija kliničkih i neurofizioloških nalaza sa kvalitetom života bolesnika sa dijabetesnom polineuropatijom

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Abstract

Background/Aim. Diabetic polyneuropathy is defined as the presence of clinical or subclinical symptoms and/or signs of peripheral nerve damage in patients with diabetes mellitus in the absence of the other causes of peripheral neuropathy. The aim of this study was to assess health-related quality of life (HRQoL) in patients with diabetic polyneuropathy and its correlation with clinical and neurophysiological findings. **Methods.** This study comprised 60 patients with distal, symmetric, sensorimotor diabetic polyneuropathy and type 2 diabetes mellitus. For evaluation of clinical findings the following scales were used: Medical Research Council strenth score (MRC sum score), Inflammatory Neuropathy Cause and Treatment (INCAT) disability scale (arm disability and leg disability scales), INCAT sensory sum score, Hamilton depression and anxiety rating scales. Nerve conduction study (NCS) was performed on the motor part of the median and peroneal nerves, the sensory part of the median nerve and sural nerve. All the patients completed the Serbian version of the SF-36 questionnaire as a measure of HRQoL. **Results.** Our results showed mild to moderate QoL impairment in the patients with diabetic polyneuropathy with no difference in physical and mental composite scores ($p > 0.05$). The age of the patients, mean MRC sum score, arm disability scale score, leg disability scale score and mean INCAT sensory sum score correlated with scores in the SF-36 questionnaire ($p < 0.01$). The patients with higher scores of anxiety and depression had significantly worse health perception for all QoL domains, for both composite scores and for the total SF-36 score ($p < 0.01$). Both motor and sensory NCS parameters of the median nerve showed significant correlations with QoL scores ($p < 0.05$). **Conclusion.** Our results showed mild to moderate QoL impairment in the patients with diabetic polyneuropathy. HRQoL significantly correlated with the age of the patients, muscle strength, disability, sensory complaints, depressiveness and anxiety of the patients. Electrophysiological examination of median nerve significantly correlated with QoL in the patients with diabetic polyneuropathy.

Key words:
diabetic neuropathies; neurophysiology; quality of life; questionnaires.

Apstrakt

Uvod/Cilj. Dijabetesna polineuropatija definiše se kao prisustvo kliničkih ili supkliničkih simptoma i/ili znakova oštećenja perifernih živaca kod bolesnika sa dijabetesom melitusom u nedostatku drugih uzroka periferne neuropatije. Cilj rada bio je da se proceni kvalitet života povezan sa zdravljem (HRQoL) kod bolesnika sa dijabetesnom polineuropatijom i njegova povezanost sa kliničkim i neurofiziološkim nalazom. **Metode.** U istraživanju je učestvovalo 60 bolesnika sa distalnom simetričnom senzorimotornom dijabetesnom polineuropatijom u sklopu dijabetesa melitusa tipa 2. Za objektivnu procenu kliničkog nalaza korišćene su sledeće skale: *Medical Research Council strenth score* (MRC skor), *Inflammatory Neuropathy Cause and Treatment* (INCAT) skala invalidnosti (za ruke i noge), INCAT senzorna skala, Hamiltonova skala depresivnosti i anksioznosti. Elektroneurografija (ENG) sprovedena je na motornom delu *n. medianus*-a i *n. peroneus*-a i na senzornom delu *n. medianus*-a i na *n. suralis*-u. Svi bolesnici popunili su srpsku verziju upitnika SF-36. **Rezultati.** Registrovano je blago do umereno sniženje kvaliteta života kod bolesnika sa dijabetesnom polineuropatijom, i to bez razlika u fizičkom i mentalnom domenu ($p > 0,05$). Starost bolesnika, MRC skor, INCAT skala invalidnosti i INCAT senzorna skala bile su u korelaciji sa rezultatima na SF-36 upitniku ($p < 0,01$). Bolesnici sa višim skorom an-

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ksioznosti i depresivnosti imali su značajno lošiju percepciju zdravlja za sve domene, za oba kompozitna skora i ukupni SF-36 skor ($p < 0,01$). Motorni i senzorni ENG parametri za *n. medianus* značajno su korelisali sa HRQoL ($p < 0,05$). **Zaključak.** Naši rezultati pokazuju blago do umereno sniženje kvaliteta života kod bolesnika sa dijabetesnom polineuropatijom. Kvalitet života kod ovih bolesnika je u značajnoj vezi sa starošću bolesnika, njihovom mišićnom snagom, stepenom invalidnosti, senzornim smetnjama, depresivnošću i anksioznošću. Elektrofiziološki nalaz za *n. medianus* značajno je povezan sa kvalitetom života kod bolesnika sa dijabetesnom polineuropatijom.

Ključne reči:
dijabetesne neuropatije; neurofiziologija; kvalitet života; upitnici.

Introduction

Diabetic polyneuropathy is defined as the presence of clinical or subclinical symptoms and/or signs of peripheral nerve damage in patients with diabetes mellitus in the absence of the other causes of peripheral neuropathy [1]. It is one of the most common and most important complications of diabetes, and one of the most frequent polyneuropathies in developed countries [2, 3]. The most frequent form of diabetic polyneuropathy is distal, symmetric, sensorimotor, predominantly sensory polyneuropathy and it is encountered in 30–50% of patients with diabetes [4, 5]. It is mainly of axonal type with secondary demyelination, but with the progress of the disease it can become sensorimotor axonal-demyelinating [6, 7].

Having in mind a high prevalence of diabetes and high treatment expenses, diabetic polyneuropathy has also significant socioeconomic impact [3]. Quality of life (QoL) is worse in patients with diabetes who have complications including diabetic polyneuropathy [8–10]. Venkataraman et al. [11] even found that peripheral neuropathy, among all complications, was associated with the greatest reduction in quality of life. Diabetic patients with neuropathy also have significantly worse trajectory of QoL outcomes over time compared to patients without neuropathy [12]. Previous studies usually compared QoL in diabetic patients with and without complications, but neither of them evaluated influence of clinical and electrophysiological parameters on QoL in a cohort of patients with peripheral diabetic neuropathy.

The aim of this study was to assess QoL in patients with diabetic polyneuropathy and its correlation with clinical and neurophysiological findings.

Methods

This study comprised 60 patients with distal, symmetric, sensorimotor diabetic polyneuropathy as a complication of diabetes mellitus type 2. All the patients were diagnosed and treated at the Neurology Clinic, Clinical Center in Banja Luka, Bosnia and Herzegovina. The other etiology of polyneuropathy was excluded by additional investigations, including urea, creatinine, vitamin B12 and thyroid hormones serum levels, immunological and virusological analysis, electrophoresis of serum and urine proteins with immunofixation, tumor markers. Patients with any other severe disease or macrovascular and microvascular diabetic complications except polyneuropathy, those with cognitive failure, alcohol or drug abuse were excluded from the study. Prior to the enrolment into the study informed consent was obtained from all the patients. The study was approved by the Ethics Committee of the Neurology Clinic in Banja Luka.

A general questionnaire was used to assess demographic characteristics of the investigated patients, including gender, age at onset and duration of diabetic neuropathy, as well as current age.

For evaluation of clinical findings the following scales were used: Medical Research Council strenth score (MRC sum score), Inflammatory Neuropathy Cause and Treatment (INCAT) disability scale (arm disability and leg disability scales), and INCAT sensory sum score. The MRC sum score was calculated by summation of MRC scores for 8 muscle groups bilaterally and the overall score ranges from 0 (total paralysis) to 80 (normal strength) [13]. The arm disability scale quantifies daily activities of the arms, with the span ranging from 0 (no signs of disability) to 5 (most severe disability) [14], while the leg disability scale quantifies walking ability with the results ranging from 0 (walking is not affected) to 5 (wheelchair bound, unable to stand or walk even with help) [14]. The INCAT sensory sum score includes examination of pain and vibration sensibility in arms and legs, as well as two-point discrimination sensibility in arms. The score has values ranging from 0 (normal sensation) to 20 (most severe sensory deficit) [15, 16]. Muscle stretch reflexes of biceps and triceps, as well as patellar and Achilles reflexes were also examined. Every reflex was marked as 1 (absent), 2 (lower) or 3 (normal), so the reflex score had values ranging from 8 (generalized areflexia) to 24 (normal reflexes) [17].

For evaluation of depression, the 21-item Hamilton depression rating scale (Ham-D) was used where a score less than 8 signifies the absence of depression [18]. For evaluation of anxiety, the Hamilton anxiety rating scale (Ham-A) was used where a score less than 18 marks the absence of anxiety [19].

Electroneurography examination was performed by the single examiner on the Oxford Synergy equipment. Temperature of the examined limb was maintained above 31°C. Nerve conduction study (NCS) was performed using surface stimulation and registration electrodes on the standard positions for the examined nerves (motor part of median and peroneal nerves, sensory part of the median nerve and the sural nerve). The following parameters were assessed: motor conduction velocity (MCV), amplitude of the compound muscle action potentials (CMAP) and minimal F wave latency for motor nerves, sensory conduction velocity (SCV) and amplitude of the sensory nerve action potentials (SNAP) for sensory nerves. Polyneuropathy was defined as sensory, motor or sensorimotor according to the type of predomi-

nantly affected nerves. According to the pathophysiological mechanism of nerve damage, polyneuropathy was marked as axonal, demyelinating or axonal-demyelinating according to the criteria published by Tankisi et al. [20].

All the patients completed the Serbian version of the SF-36 questionnaire as a measure of HRQoL [21]. The SF-36 is a generic instrument that measures eight general health concepts: physical functioning (PF), role physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role emotional (RE) and mental health (MH). Two main scores are available to summarize these scales: physical composite score (PCS) and mental composite score (MCS), as well as total SF-36 score. All these scores fall within a 0–100 scale, with higher scores reflecting better HRQoL.

Statistical analysis included descriptive statistics, Man Whitney U-test, Student's *t*-test, ANOVA and Spearman correlation analysis. Significant testing was two-sided, with alpha sets at 0.05 for a statistical significance and 0.01 for a high statistical significance.

Results

The results of the SF-36 questionnaire are shown in Figure 1. The best subscore was found for PF and the worse for GH. There was no difference in PCS and MCS ($p > 0.05$).

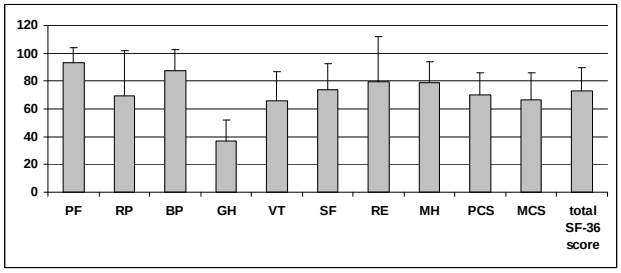

Fig. 1 – Results of the SF-36 questionnaire in the patients with diabetic polyneuropathy in all domains (n = 60). The results are shown as x̄ ± standard deviation.

PF – physical functioning; RP – role physical; BP – bodily pain; GH –general health; VT – vitality; SF – social functioning; RE – role emotional; MH – mental health; PCS – physical composite score; MCS – mental composite score.

Demographic data and therapeutic approach in the analyzed patients are shown in Table 1. There was no difference in QoL regarding gender of the patients ($p > 0.05$). Those older at the onset of the disease had significantly lower RP, BP and VT subscores, as well as PCS and the total SF-36 score ($p < 0.05$). There was no correlation between duration of diabetic neuropathy and QoL measured by the SF-36 ($p > 0.05$). The age of the patients significantly correlated with RP, BP, VT, PCS, the total SF-36 score ($p < 0.01$), as well as with GH and MCS ($p < 0.05$).

Table 1

Sociodemographic characteristics and therapeutic approach in the analyzed patients with diabetic polyneuropathy

Demographic characteristics (n = 60)	Values
Sex (%)	
male	50.0
female	50.0
Age at onset, years (mean years ± SD)	44.3 ± 12.0
Current age, years (mean years ± SD)	56.5 ± 9.9
Duration of disease (mean years ± SD)	12.2 ± 6.0
Type of therapy (%)	
only oral hypoglycemics	33.3
insulin	66.7
Hemoglobin A1c (%)	7.3 ± 2.3

The mean MRC sum score of the analyzed patients with diabetic polyneuropathy was 78.2 ± 4.5. The arm disability scale score was 0.13 ± 0.39, leg disability scale score 0.23 ± 0.46 and mean INCAT sensory sum score 2.35 ± 2.53. All these scores correlated with better scores on each domain of SF-36 questionnaire ($p < 0.01$) (Table 2). Mean muscle stretch reflexes score was 17.7 ± 4.7 and it correlated with VT, SF, RE, MH, PCS, MCS and total SF-36 score ($p < 0.01$), as well as with PF, RP and GH ($p < 0.05$).

The average Ham-D score was 4.58 ± 3.76, while average Ham-A was 2.71 ± 2.29. The patients with higher scores of anxiety and depression had significantly worse health perception for all QoL domains, for both composite scores and for the total SF-36 score ($p < 0.01$) (Table 2).

Table 2

Correlation between clinical factors and quality of life (QoL) in the patients with diabetic polyneuropathy (n = 60)

SF-36 domains	MRC sum score	INCAT Arm disability scale	INCAT Leg disability scale	INCAT Sensory sum score	Muscle stretch reflexes score	Ham-D score	Ham-A score
PF	0.609; 0.001	-0.470; 0.001	-0.601; 0.001	-0.508; 0.001	0.294; 0.023	-0.642; 0.001	-0.593; 0.001
RP	0.529; 0.001	-0.513; 0.001	-0.518; 0.001	-0.399; 0.002	0.327; 0.011	-0.468; 0.001	-0.413; 0.001
BP	0.331; 0.010	-0.326; 0.011	-0.393; 0.002	-0.350; 0.006	0.240; 0.065	-0.483; 0.001	-0.479; 0.001
GH	0.386; 0.002	-0.412; 0.001	-0.452; 0.001	-0.414; 0.001	0.299; 0.020	-0.777; 0.001	-0.735; 0.001
VT	0.461; 0.001	-0.417; 0.001	-0.516; 0.001	-0.477; 0.001	0.418; 0.001	-0.824; 0.001	-0.781; 0.001
SF	0.395; 0.002	-0.439; 0.001	-0.501; 0.001	-0.422; 0.001	0.362; 0.005	-0.843; 0.001	-0.793; 0.001
RE	0.360; 0.005	-0.366; 0.004	-0.343; 0.007	-0.385; 0.002	0.402; 0.001	-0.819; 0.001	-0.782; 0.001
MH	0.344; 0.007	-0.414; 0.001	-0.414; 0.001	-0.368; 0.004	0.372; 0.003	-0.804; 0.001	-0.793; 0.001
PCS	0.521; 0.001	-0.460; 0.001	-0.561; 0.001	-0.497; 0.001	0.399; 0.002	-0.752; 0.001	-0.700; 0.001
MCS	0.394; 0.002	-0.413; 0.001	-0.450; 0.001	-0.457; 0.001	0.370; 0.004	-0.902; 0.001	-0.854; 0.001
Total SF-36	0.462; 0.001	-0.442; 0.001	-0.502; 0.001	-0.479; 0.001	0.380; 0.003	-0.862; 0.001	-0.807; 0.001

The results are shown as Spearman's rho; MRC – Medical Research Council strenth score; INCAT – Inflammatory Neuropathy Cause and Treatment; HAM – Hamilton depression (D) or anxiety (A) rating scale; PF – physical functioning; RP – role physical; BP – bodily pain; GH –general health; VT – vitality; SF – social functioning; RE – role emotional; MH – mental health; PCS – physical composite score; MCS – mental composite score.

The results of NCS in our patients with diabetic polyneuropathy are presented in Table 3. Regarding NCS parameters of the motor peroneal nerve, only MCV was in correlation with PF domain (rho = 0.336, $p < 0.009$). Regarding sural nerve, only SNAP amplitude correlated with VT domain (rho = 0.30, $p = 0.013$). Both motor and sensory NCS parameters of median nerve showed significant correlations with QoL scores (Table 4).

Table 3

Nerve conduction study findings in the patients with diabetic polyneuropathy (n = 60)

Investigated nerve conduction parameters	Value ($\bar{x} \pm SD$)
Median nerve (motor part)	
MCV (m/s)	49.77 ± 4.08
CMAP amplitude (mV)	9.18 ± 1.75
F wave latency (m/s)	30.72 ± 2.31
Peroneal nerve	
MCV (m/s)	39.49 ± 4.00
CMAP amplitude (mV)	4.23 ± 1.84
F wave latency (m/s)	56.92 ± 5.62
Median nerve (sensory part)	
SCV (m/s)	46.44 ± 4.71
SNAP amplitude (μV)	9.52 ± 6.54
Sural nerve	
SCV (m/s)	35.89 ± 5.57
SNAP amplitude (μV)	2.80 ± 1.41

MCV– motor conduction velocity; CMAP – compound muscle action potentials; SCV – sensory conduction velocity; SNAP – sensory nerve action potentials.

QoL, especially in patients with diabetic complications including polyneuropathy [9–12]. Physical and mental domains were similarly affected in our patients which is in accordance with few previous studies [22, 23]. This fact signifies the importance of QoL measure in diabetic polyneuropathy since physicians are usually focused on physical symptoms and have neglect for patients' subjective complaints. In line with this observation, we registered the lowest scores for GH and VT domains which is in accordance with other studies [23–25], and it further speaks in favor of the importance of the mental health impairment in patients with diabetic polyneuropathy.

In our study, the patients of older age at onset of the disease and at the moment of investigation had worse health-related QoL, particularly for physical domains. On the other hand, duration of disease did not affect any subscore of QoL. Similar results were published by Lloyd et al [22]. Both findings mean that QoL was in association with normal ageing process but not with duration of diabetic neuropathy itself. On the other hand, there are also publications that showed worse PCS in patients with longer duration of disease [23], but we failed to find this correlation.

According to our results, clinical parameters of severity of diabetic polyneuropathy were in a significant correlation with SF-36 scores. Although muscle strength was pretty good in our patients and disability of arms and legs was minor, these parameters significantly affected all aspects of QoL. Similarly,

Table 4

Correlation between nerve conduction study of the median nerve and quality of life in the patients with diabetic polyneuropathy (n = 60)

SF-36 domains	Motor part of median nerve			Sensory part of median nerve	
	MCV	CMAP amplitude	F wave latency	SCV	SNAP amplitude
PF	0.285; 0.028	0.332; 0.009	-0.501; 0.001	0.560; 0.001	0.318; 0.013
RP	0.048; 0.714	0.221; 0.090	-0.364; 0.004	0.172; 0.189	0.332; 0.010
BP	0.112; 0.395	0.271; 0.037	-0.283; 0.029	0.212; 0.104	0.349; 0.006
GH	0.114; 0.386	0.323; 0.012	-0.236; 0.069	0.181; 0.166	0.423; 0.001
VT	0.154; 0.240	0.286; 0.027	-0.231; 0.076	0.274; 0.034	0.427; 0.001
SF	0.207; 0.113	0.296; 0.021	-0.350; 0.006	0.325; 0.011	0.470; 0.001
RE	0.247; 0.058	0.365; 0.004	-0.129; 0.325	0.319; 0.013	0.300; 0.020
MH	0.133; 0.312	0.268; 0.039	-0.147; 0.264	0.213; 0.102	0.364; 0.004
PCS	0.141; 0.282	0.325; 0.011	-0.383; 0.003	0.289; 0.021	0.438; 0.001
MCS	0.199; 0.128	0.341; 0.008	-0.228; 0.080	0.299; 0.020	0.420; 0.001
Total SF-36	0.185; 0.156	0.353; 0.006	-0.320; 0.013	0.321; 0.012	0.444; 0.001

The results are shown as Spearman's rho; *p*. MCV – motor conduction velocity; CMAP – compound muscle action potentials; SCV – sensory conduction velocity; SNAP – sensory nerve action potentials. PF – physical functioning; RP – role physical; BP – bodily pain; GH –general health; VT – vitality; SF – social functioning; RE – role emotional; MH – mental health; PCS – physical composite score; MCS – mental composite score.

Sensorimotor polyneuropathy was diagnosed in 51 (85%) of the patients and sensory polyneuropathy in 9 (15%). Forty four (73.3%) patients had axonal and 16 (26.7%) patients had axonal-demyelinating polyneuropathy. The patients with sensorimotor polyneuropathy had similar SF-36 scores as patients with pure sensory polyneuropathy ($p > 0.05$). Also, the patients with axonal-demyelinating polyneuropathy had similar QoL like those with pure axonal polyneuropathy ($p > 0.05$).

Discussion

Our results show mild to moderate QoL impairment in the patients with diabetic polyneuropathy. Previous studies showed that diabetes had mild to moderate influence on better QoL was associated with higher values of the MRC sum score and lower INCAT disability scores in patients with immune mediated polyneuropathies [15, 26]. Sensory symptoms were more common than motor in our patients with diabetic neuropathy and their influence on all the aspects of QoL was obvious. According to literature data, patients with immune mediated neuropathies who had higher values of INCAT sensory composite score had worse results for PF, BP and PCS [26, 27]. Thus, sensory complaints may have significant impact on QoL in patients with neuropathies and they should not be neglected by physicians. Finally, we found that even examination of muscle stretch reflexes may be suggestive of worse QoL but this factor was the least important clinical parameter for estimation of QoL in diabetic polyneuropathy.

Mean Ham-D and Ham-A scores were pretty low in our study which is in accordance with previous finding that depressiveness and anxiety are present in only about one third of patients with diabetes [9, 28, 29]. Besides this, our patients with higher scores of anxiety and depression had significantly worse perception of health-related QoL. Similar results were published previously for diabetic patients [30]. Psychological and pharmacological treatment of depression and anxiety may lead to better blood sugar control, better functional status and better perception of QoL in patients with diabetic neuropathy [31].

Established correlations between electrophysiological parameters and QoL are very important since NCS is an objective measure of diabetic polyneuropathy more sensitive than clinical examination [32]. Lower QoL was previously found even in subclinical forms of polyneuropathy diagnosed only by electromyography but not by clinical examination [33]. Certain inconsistent correlations between NCS parameters of peroneal and sural nerves with QoL were found in our and a study by Padua et al. [23]. On the other hand, according to our data NCS findings on the median nerve were more important to estimate QoL in patients with diabetic polyneuropathy. The most significant correlations were observed between CMAP amplitude and QoL, as well as between SNAP amplitude and QoL. This means that axonal damage of the median nerve may be suggestive of worse QoL. This may be explained that nerves of upper extremities are affected later in the course of the disease and that median nerve impairment may lead to severe arm disability including using of tool, writing, driving, clothing etc.

Previous studies reported lower QoL scores in patients with sensorimotor compared to those with sensory polyneuropathy and in axonal-demyelinating compared to axonal type of polyneuropathy [32]. This correlation seems logical and may be explained by natural progression of disease. However, we failed to find these correlations which can be explained with small sample analyzed.

Conclusion

Our results show mild to moderate quality of life (QoL) impairment in the patients with diabetic polyneuropathy. Besides, the age of the patients, muscle strength and disability, sensory complaints also had great influence on QoL. The patients with higher level of anxiety and depressiveness had significantly worse perception of health-related QoL. The most prominent finding in our study is that electrophysiological examination of the median nerve significantly correlates with QoL in the patients with diabetic polyneuropathy.

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